What is claimed is:

5

10

15

20

25

30

- A process for preparing enantiomerically enriched (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol from racemic (4bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol, comprising:
- (a) converting said racemic (4-bromo-2-(hydroxymethyl)phenyl)-(4fluorophenyl)methanol to a racemic monoester intermediate by reaction with a carboxylic acid or a reactive derivative thereof;
 - reacting said racemic monoester intermediate with an optically active acid to form a salt of said racemic monoester intermediate;
 - (c) crystallization of said salt to recover an enantiomerically enriched, crystalline form of said salt;
 - (d) neutralization of said salt to give an enantiomerically enriched form of said monoester intermediate; and
 - (e) hydrolysis of the enantiomerically enriched form of said monoester intermediate to produce said enantiomerically enriched (4-bromo-2-(hydroxymethyl)phenyl)-(4fluorophenyl)methanol.
- 2. The process of claim 1, wherein the (4-bromo-2- (hydroxymethyl)phenyl)-(4-fluorophenyl)methanol produced in step (e) is enriched in an enantiomer which can be converted to escitalopram by dehydration and by substitution of bromine by a nitrile group.
- 3. The process of claim 1 or 2, wherein step (a) comprises reaction of

said racemic (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol with a reactive derivative of a carboxylic acid, said reactive derivative being selected from the group comprising acid chlorides and acid anhydrides.

5

10

- 4. The process of claim 3, wherein said step (a) comprises reaction of said racemic (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol with acetic anhydride to form the monoacetate ester of said racemic (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol.
- 5. The process of claim 1, wherein said optically active acid is di-p-toluoyl tartaric acid.
- 15 6. The process of claim 5, wherein said optically active acid is (+)-di-p-toluoyl tartaric acid.
 - 7. The monoacetate ester of (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol and salts thereof.

20

- 8. An enantiomerically enriched monoacetate ester of (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol and salts thereof.
- The ester of claim 8, being enriched in an enantiomer which can be
 converted to escitalopram by dehydration and by substitution of bromine by a nitrile group.
 - 10. The ester of claim 9, wherein said salt is the (+)-di-p-toluoyl tartaric acid salt of said monoacetate ester.

30

11. A process for preparing escitalopram, comprising:

WO 03/087081

20

25

- (a) reacting 5-bromophthalide with 4-fluoro-phenylmagnesium bromide to produce 4-bromo-2-hydroxymethyl-4'-fluorobenzophenone;
- 5 (b) reacting said 4-bromo-2-hydroxymethyl-4'-fluorobenzophenone with 3-dimethylaminopropyl magnesium chloride to produce racemic (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol;
- (c) converting said racemic (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol to a racemic monoester intermediate by reaction with a carboxylic acid or a reactive derivative thereof;
- (d) reacting said racemic monoester intermediate with an optically
 active acid to form a salt of said racemic monoester intermediate;
 - (e) crystallization of said salt to recover an enantiomerically enriched, crystalline form of said salt;
 - (f) neutralization of said salt to give an enantiomerically enriched form of said monoester intermediate;
 - (g) hydrolysis of the enantiomerically enriched form of said monoester intermediate to produce enantiomerically enriched (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol;
- (h) dehydration of said enantiomerically enriched (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol to produce
 30 enantiomerically enriched 1-(4'-fluorophenyl)-1-(3-dimethylaminopropyl)-5-bromophthalane; and

WO 03/087081 PCT/CA03/00522

-20-

- (i) replacement of bromine by a nitrile group to produce escitalopram.
- The process of claim 11, wherein step (c) comprises reaction of said racemic (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol with a reactive derivative of a carboxylic acid, said reactive derivative being selected from the group comprising acid chlorides and acid anhydrides.
- 10 13. The process of claim 12, wherein said step (c) comprises reaction of said racemic (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol with acetic anhydride to form the monoacetate ester of said racemic (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol.

15

- 14. The process of claim 11, wherein said optically active acid is di-p-toluoyl tartaric acid.
- 15. The process of claim 14, wherein said optically active acid is (+)-di-p-toluoyl tartaric acid.